

PTSA-catalyzed green synthesis of 1,3,5-triarylbenzene under solvent-free conditions†

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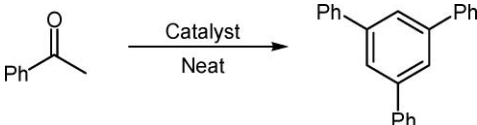
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An economical and green conversion of acetophenones into 1,3,5-triarylbenzenes catalyzed by PTSA is described. The present method is facile and chemo-selective without using any metal catalyst or solvent.

Screening green methods for chemical synthesis is urgent and challenging in the long term to avoid the adverse consequences of the substances used and generated.¹ A green chemical process for sustainable development always involves considerations such as using cost-effective catalysts without any additives, employing water as a solvent or with a solvent-free system. In addition, a simple workup procedure is also desirable.

1,3,5-Triarylbenzenes are very useful compounds used as electroluminescing materials, electrode devices,² resisting materials³ or conducting polymers.⁴ These compounds can also serve as versatile intermediates for the synthesis of buckminsterfullerenes, pharmaceuticals and conjugated star polyaromatics.⁵ As a result, the synthesis of 1,3,5-triarylbenzenes has attracted much attention and a variety of methodologies have been developed. To our knowledge, triple condensations of alkynes catalyzed by transition metal complexes (such as Nb,⁶ Co,⁷ Ir,⁸ Pd⁹ and Rh¹⁰) have been widely investigated. Metal-catalysed cross-coupling reactions between 1,3,5-trihalobenzenes with organometallic partners also act as an alternative.¹¹ Of the methodologies mentioned above, however, alkynes are somewhat expensive and not readily available. Meanwhile, the triple self-condensation of alkynes always involves precious metal catalysts together with ligands.^{6–10} Moreover, the triple condensation of alkynes always produces 1,3,5-triarylbenzenes as minor products or by-products.^{7,8,9,10} Comparatively, cross-coupling reactions from 1,3,5-trihalobenzenes can give better yields without the employment of precious metals. On the other hand, syntheses of 1,3,5-triarylbenzenes from aryl methyl ketones have been regarded as more straightforward methods and many methodologies have been developed.^{2,12,13} Of these protocols used in this manner, however, most suffer from using precious metal catalysts, lower yields or harsh operating conditions. Due to their expensive nature, inadequate accessibility, toxicity of the additives often used and the generation of toxic waste as well as

Table 1 Catalyst and temperature screening for the triple condensation of **1a**^a

				
Entry	Catalyst	Temperature/°C	Time/h	Yield (%) ^b
1	FeCl ₃	130	10	65 ^c
2	FeCl ₃	130	10	78
3	ZnCl ₂	130	10	40
4	CuCl ₂	130	10	38
5	CAN	130	10	>10
6	TiCl ₄	130	10	50
7	Fe ₃ O ₄	130	10	0
8	I ₂	130	10	0
9	TsOH·H ₂ O	130	10	85
10	TsOH·H ₂ O	130	10	91 ^d
11	TsOH·H ₂ O	80	12	^e
12	TsOH·H ₂ O	rt	24	0

^a Conditions: **1** (3 mmol), catalyst (5 mol%), solvent free. ^b Isolated yield. ^c 2% catalyst was used. ^d 10% catalyst was used. ^e Trace product was obtained.

the use of organic solvent, there is an urgent need to develop a powerful method to meet the requirement of green chemistry.

More recently, PTSA (TsOH·H₂O) has attracted much attention from synthetic organic chemists and has been extensively applied for a plethora of organic transformations¹⁴ because of its relative nontoxicity, ready availability, and is fairly insensitive. As a continuation of our ongoing efforts to explore environmentally benign synthetic reactions,¹⁵ herein we wish to report a simple and green method for the synthesis of 1,3,5-triarylbenzenes from aryl methyl ketone catalyzed by PTSA under solvent-free conditions.

Initially, we chose acetophenone **1a** as the model substrate. Firstly, the reaction was carried out in the presence of FeCl₃ (2%) under solvent-free conditions (Table 1, entry 1). To our delight, a large amount of 1,3,5-triphenylbenzene was afforded as white solid.¹¹ Since Fumiaki Ono *et al.*² didn't obtain the same product using FeCl₃, AlCl₃ or TiCl₄ in toluene under reflux, we thus deduced the presence of solvent may disfavor the triple condensation. When 5% FeCl₃ was used, the above conversion got a substantial increase to 78% yield (Table 1, entry 2). A variety of experimental parameters including catalysts and their loadings were screened to optimize the reaction conditions. Many other catalysts such as I₂, ZnCl₂, CuCl₂, TiCl₄, (NH₄)₂Ce(NO₃)₆ and Fe₃O₄ were also tested for this transformation, only to produce

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Table 2 Cyclotrimerization of aryl methyl ketone catalyzed by TsOH·H₂O^a

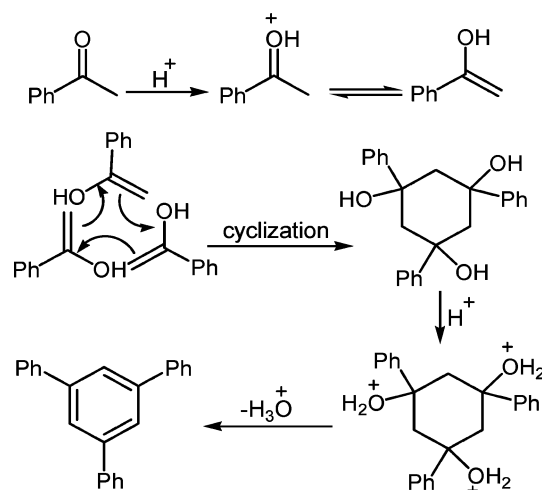
Entry	Ar	Product	Temperature/°C	Time/h	Yield (%) ^b
1	C ₆ H ₅	2a	130	10	91
2	<i>p</i> -CH ₃ C ₆ H ₄	2b	146	13	87
3	<i>p</i> -NH ₂ C ₆ H ₄	2c	142	16	71
4	<i>p</i> -OCH ₃ C ₆ H ₄	2d	148	25	68
5	<i>p</i> -NO ₂ C ₆ H ₄	2e	140	24	- ^c
6	<i>p</i> -FC ₆ H ₄	2f	143	24	90
7	<i>p</i> -ClC ₆ H ₄	2g	145	13	74
8	<i>p</i> -BrC ₆ H ₄	2h	130	18	82
9	<i>p</i> -IC ₆ H ₄	2i	128	22	84
10	<i>o</i> -CH ₃ C ₆ H ₄	2j	136	24	70
11	<i>m</i> -CH ₃ C ₆ H ₄	2k	140	18	85
12	<i>m</i> -ClC ₆ H ₄	2l	145	16	71
13	<i>o</i> -ClC ₆ H ₄	2m	146	19	61

^a Conditions: 3 mmol of aryl methyl ketone, 0.3 mmol of TsOH·H₂O, no solvent. ^b Isolated yields. ^c No reaction.

somewhat lower yields (Table 1, entries 3–8). However, the triple condensation reaction became quite sluggish with poor yields when *p*-OCH₃ and *o*-CH₃ substituted acetophenones were used. Elevating the reaction temperature didn't bring any improvement. To solve this problem, we paid attention to other new catalysts. Fortunately, the reaction afforded an 85% yield of **2a** using 5% PTSA. Using 10% PTSA (TsOH·H₂O), the yield was enhanced to 91%. Effect of reaction temperature was also studied, and the results showed that lower temperatures disfavored the reaction (Table 1, entries 10–12).

After optimization of conditions, we investigated the scope and the limitation of this trimerization reaction. As shown in Table 2, acetophenones containing either electron-donating or electron-withdrawing groups reacted smoothly to afford 1,3,5-arylbenzenes in good yields. When the *para*-substituents were chloro, bromo and iodo, the yields increased as their electronegativity decreased (Table 2, entries 7, 8, 9). On the other hand, strong electron-donating groups such as -NH₂ and -OCH₃ provided lower yields (Table 2, entry 3, 4) than other groups such as alkyls or halogens. When substrates with a strong electron-withdrawing nitro group were used, no reaction occurred even after enhancing the loading of TsOH·H₂O to 1 equivalent (Table 2, entry 5). The steric effect was significant, and the reactions of *para*- or *meta*-substituted chloroacetophenones afford little higher yields than sterically hindered *ortho*-substituted acetophenone. The results also indicate the reactivity order of substituted acetophenones: *para*- > *meta*- > *ortho*- (Table 2, entries 2, 7, 10, 11, 12, 13).

As to the mechanism, a possible procedure for the cyclotrimerization of acetophenones is described below. As shown in Scheme 1, epimerization of protonated acetophenone provided the corresponding enol form. Subsequent cyclization of three monomers (enol form) led to the formation of substituted cyclophloroglucinol. Final dehydration of substituted cyclophloroglucinol afforded the 1,3,5-triphenylbenzene deriva-

**Scheme 1** Possible mechanism for the cyclotrimerization of acetophenones.

tives. Importantly, water was the only by-product in the whole process, which added to its attractiveness.

In conclusion, we have developed a simple and green method for the synthesis of 1,3,5-triarylbenzenes catalyzed by PTSA under solvent-free conditions.¹⁶ The major advantages of the method lie in the cheap catalyst, easy work up and avoidance of using harmful solvent. This could be an economical protocol for the preparation of 1,3,5-arylbenzenes compared with other reported methods. Furthermore, water is afforded as the by-product in this reaction, which makes the present process environmentally benign.

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- 16 General procedure: To a 15 mL two necked round bottom bottle, 360.45 mg (3 mmol) of acetophenone **1a** and 57.07 mg (0.30 mmol) of TsOH·H₂O was added. The reaction mixture was stirred at 130 °C for 10 h, determined by TLC. After completion of the reaction, the reaction mixture was neutralized by saturated NaHCO₃, extracted with DCM (3 x 20 mL) or ethyl acetate (3 x 50 mL). The combined organic layers were dried by MgSO₄, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 20:1) and gave 278.82 mg (0.91 mmol, 91%) of **2a**, as white solid.